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Veno-Arterial Extracorporeal Membrane Oxygenation after Surgical Repair of Type A Aortic Dissection

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Veno-Arterial Extracorporeal Membrane Oxygenation after Surgical Repair of Type A Aortic Dissection

Running title: VA-ECMO in aortic dissection

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Abstract

Veno-arterial (VA) extracorporeal membrane oxygenation (ECMO) support for postcardiotomy cardiogenic shock (PCS) in patients undergoing surgery for acute type A aortic dissection (TAAD) is controversial and the available evidence is confined to limited case series. We aimed to evaluate the impact of this salvage therapy in this patient population. Between January 2010 and March 2018, all TAAD patients receiving VA-ECMO for PCS were retrieved from the PC-ECMO registry. Hospital mortality and other secondary outcomes were compared with PCS patients undergoing surgery for other cardiac pathologies and treated with VA-ECMO. Among the 781 patients in the PC-ECMO registry, 62 (7.9%) underwent TAAD repair and required VA-ECMO support for PCS. In-hospital mortality accounted for 46 (74.2%) patients, while 23 (37.1%) were successfully weaned from VA-ECMO. No significant differences were observed between the TAAD and non-TAAD cohorts with reference to in-hospital mortality (74.2 vs 63.4%, p = 0.089). However, patients in the TAAD group had a higher rate of neurological events (33.9 vs 17.6%, p = 0.002), but similar rates of reoperation for bleeding/tamponade (48.4 vs 41.5%, p = 0.29), transfusion of ≥10 red blood cell units (77.4 vs 69.5%, p = 0.19), new-onset dialysis (56.7 vs 53.1%, p = 0.56), and other secondary outcomes.

VA-ECMO provides a valid support for patients affected by PCS after surgery for TAAD.

Trial Registration: Clinicaltrials.gov - NCT03508505

Keywords: Extracorporeal membrane oxygenation; ECMO, ECLS; Postcardiotomy; Cardiac surgery; Heart failure; Aortic dissection.

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Introduction

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) provides temporary mechanical circulatory support for patients affected by postcardiotomy cardiogenic shock (PCS), allowing for cardiopulmonary recovery.[1,2] However, complications and mortality rates after postcardiotomy VA-ECMO remain high, with reported successful weaning from VA-ECMO and hospital mortality between 40% to 70%, and 50 to 80%, respectively.[2-6] Therefore, selection of patients requiring VA-ECMO is a crucial element for a successful postoperative outcome. In this context, the efficacy of VA-ECMO in patients undergoing surgery for acute type A aortic dissection (TAAD) is controversial, and available data is confined to limited case series.[7-10] We report the outcome of patients with PCS following TAAD repair from the multicentre Postcardiotomy Veno-arterial Extracorporeal Membrane Oxygenation (PC-ECMO) registry.

Methods

The patient population was collected from the observational, multicenter PC-ECMO registry that enrolled patients undergoing VA-ECMO following adult cardiac surgery at 19 centers from Belgium, Czech Republic, Finland, France, Germany, Italy, Saudi Araba, Sweden, and the United Kingdom from January 2010 to March 2018. The present study is registered at http://www.clinicaltrials.gov (unique identifier: NCT03508505) and was approved by local or regional Institutional Review Boards, where applicable. The detailed protocol with definition criteria has been published previously.[6] The study complies with the Strengthening the Reporting of Observational Studies in Epidemiology reporting requirements for observational studies (Table I in the Data Supplement).[11]

Only patients affected by PCS following TAAD repair requiring VA-ECMO support were included in this analysis. Baseline characteristics, demographics, comorbidities, intraoperative factors, postoperative outcomes, and VA-ECMO related data were recorded, and variable definitions have been previously reported.[6] The main outcome measure was in-hospital mortality, while secondary outcomes included death on VA-ECMO, reoperation for bleeding/tamponade, postoperative neurological and renal complications, sternal wound infection, red blood cell transfusion, and the length of stay in hospital and the intensive care unit.

Statistical analyses were performed using the SPSS statistical software v. 24.0 (IBM Corporation, Armonk, NY, USA), and Stata v. 15.1 (SAS Institute Inc., Cary, NC, USA). Covariates and outcomes were reported as counts and percentages, and as mean and standard deviation or median and interquartile range (IQR). The Mann-Whitney U, chi-square, and Fisher's exact tests were used for univariate analysis. The impact of aortic dissection on hospital mortality was adjusted for the PC-ECMO score[6] in the logistic regression analysis. A $p<0.05$ was set for statistical significance.

Results

Among the 781 patients of the PC-ECMO registry, 62 (7.9%) underwent TAAD repair and required VA-ECMO support for PCS. Mean age was 62.9 ± 11.0 years (range: 33-79 years) and 17 (27.4%) were female patients. When compared with patients without TAAD diagnosis, those affected by TAAD did not differ in their demographics or comorbidity profile (Table 1). The two groups exhibited significant differences in reference to cardiac presentation, duration and type of operation, which significantly increased their risk profile (Tables 1 and 2). Moreover, patients undergoing TAAD repair had higher lactate levels before VA-ECMO institution (8.6 ± 4.8 mmol/L vs 6.8 ± 4.7 mmol/L, $p=0.002$), and ECMO support was more often started immediately after surgery (74.2% vs 59.5%, $p=0.023$). Outcomes are summarized in Table 3.

Twenty-three (37.1%) patients were successfully weaned from VA-ECMO, and in-hospital mortality accounted for 46 (74.2%) patients, with no statistical difference when VA-ECMO was instituted immediately after surgery or later (76.1% versus 68.8%, $P=0.74$). Also, no differences were observed between the TAAD and non-TAAD cohorts in reference to in-hospital mortality (74.2% vs 63.4%, $p=0.089$). Patients in the TAAD group had a higher rate of neurological events (33.9% vs 17.6%, $p=0.002$), but similar rates of reoperation for bleeding/tamponade ($p=0.29$), RBC transfusion ($p=0.19$), renal failure ($p=0.56$), and other analysed secondary outcomes. In-hospital mortality did not differ even when adjusted for preoperative neurological events (OR 0.39, 95%CI 0.82-2.71) and for the PC-ECMO score (OR 0.892, 95%CI 0.46-1.73). Conversely, the TAAD cohort experienced a lower hospital and intensive care unit stay (11.9 ± 16.9 days vs 17.6 ± 18.3 days, $p<0.0001$, and 16.6 ± 27.8 days vs 25.8 ± 31.7 days, $p<0.0001$) (Table 3). However, when patients who survived were

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considered alone, , no differences in hospital and intensive care unit stay were observed (28.1 ± 23.6 vs 27.9 ± 21.5 days, p=0.74, and 45.1 ± 41.3 vs 47.5 ± 39.1 days, p=0.32, respectively).

Discussion

The present study is the largest analysis on the impact of VA-ECMO on the survival of patients with PCS after TAAD repair. In this cohort of patients, VA-ECMO proved to be a valid rescue option with similar hospital mortality and postoperative outcomes to other PCS patients who underwent surgery for other cardiac pathologies. This finding is of relevance since the use of intra-aortic balloon pump is contraindicated in those who underwent TAAD repair who develop PCS due to the coexistence of descending thoracic and abdominal aorta dissection.[7,12,13] Therefore, in this cohort of patients, VA-ECMO is the only temporary circulatory support strategy available.

Despite the fact that VA-ECMO is a well-established hemodynamic rescue option for cardiogenic shock, acute myocarditis, PCS or periprocedural support in acute decompensated heart failure, its role in postoperative TAAD setting remains controversial, and the available evidence from literature remains undoubtedly limited.[7-10] The evaluation of the outcome of PCS in this patient population is of significant value as TAAD patients have an inherently high operative risk, and surgical repair for TAAD is rather complex and involve a prolonged period of myocardial ischemia, cardiopulmonary bypass and the use of hypothermic circulatory arrest. In addition, TAAD surgical repair is often complicated by severe end-organ injury other than heart failure. Furthermore, fragile tissues and prolonged surgery may result in excessive bleeding, which may further aggravate the recovery of patients affected by TAAD. Sultan et al.[8] retrospectively reviewed TAAD patients undergoing surgical repair and VA-ECMO implantation over a 10-year period. Thirty-five TAAD cases were identified, and the observed in-hospital mortality was 88.6%, leading to questioning the use of VA-ECMO in this cohort of patients.[8]

Conversely, Lin et al.[9] demonstrated that VA-ECMO was a reasonable treatment for TAAD patients with refractory postcardiotomy cardiac failure. They compared TAAD patients requiring postoperative VA-ECMO support to those who did not, and 20 (12.3%) patients among a total of 162 required ECMO support. Although observed mortality was significantly higher in the cohort requiring VA-ECMO support (65% vs. 8.5%), long-term survival was comparable between the study groups.[9]

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Finally, Wang et al.[10] analysed 246 consecutive TAAD patients with seven patients supported postoperatively by VA-ECMO for refractory cardiogenic shock. Among those, only one patient died, leading the authors to conclude that ECMO provides good temporary cardiopulmonary support even in this high-risk patient population. Our data corroborate this evidence. TAAD patients who developed PCS and were treated with VA-ECMO had significant operative mortality, which was comparable to that of the second cohort of patients who underwent surgery for other cardiac pathologies and required postcardiotomy VA-ECMO. This proves that the occurrence of PCS rather than the type of surgery has an impact on the outcome.[1,2] In fact, a recent large multicenter study on VA-ECMO that included more than 8000 patients affected by cardiogenic shock, showed a remarkable increase of more than 30-fold in the use of VA-ECMO, but with unaltered in-hospital mortality.[2] Similarly, in the PC-ECMO registry, the year of operation did not have any impact on perioperative outcomes, with an equivalent in-hospital mortality over a 9-year period.[5]

Between the two patient cohorts, no differences were observed in reference to postoperative reoperation for bleeding/tamponade and blood transfusion rates. Although TAAD patients are intrinsically associated with longer cardiopulmonary bypass times and higher blood product transfusion demands, VA-ECMO support did not increase the risk of postoperative bleeding or the related sequelae of multiorgan failure and infections in comparison with other PCS patients undergoing cardiac surgery for other pathologies.[14,15] As expected, neurological events differed between the two groups, where patients in the TAAD group were more often subjected to preoperative neurological insult, and this risk is further increased by the use of circulatory arrest and/or selective cerebral perfusion.[14]

Another interesting finding of the present study is the shorter intensive care unit stay and hospitalization in the TAAD cohort. A plausible explanation is related to the critical status of these patients at presentation, including life-threatening conditions, for instance, organ malperfusion, acute myocardial infarction and cerebrovascular accidents.[14] This can overcome the benefit of the short-term

VA-ECMO support. As a matter of fact, the TAAD cohort required a more immediate VA-ECMO implantation and a shorter duration of the mechanical support. Another possible explanation is the fact that some of TAAD patients presenting with acute cardiac failure and myocardial stunning and promptly supported by VA-ECMO, rapidly return to almost a normal cardiac function after surgery.[9] It

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is not a surprise that after this critical early postoperative period, survival rates are similar between TAAD patients supported by VA-ECMO and other non-ECMO surgical patients.[9]

Our study has several limitations. Firstly, inherent bias to the observational nature of the present series cannot be excluded. The PC-ECMO registry includes a consecutive series of patients treated in university hospitals and regional tertiary hospitals in different European countries, possibly leading to the enrolment of a more inclusive patient population undergoing TAAD repair in centers with different referral pathways, preoperative selection criteria, and treatment strategies which makes the present results generalizable in different healthcare systems. Secondly, because the observational nature of this registry, which included only patients who underwent postcardiotomy VA-ECMO, we were not able to compare the outcome of patients with TAAD requiring VA-ECMO with those not requiring VA-ECMO support. Lastly, the sample size of our series remains small for an adequate and detailed sub-group analyses. Despite these limitations, our cohort is currently the largest available series and provides new data on the potential benefits of using VA-ECMO in TAAD patients affected by postoperative PCS.

In conclusion, our study demonstrated that VA-ECMO is a valid treatment strategy for patients undergoing surgery for acute type A aortic dissection and affected by postcardiotomy cardiogenic shock. Mortality and other secondary outcomes, including the risk of postoperative bleeding, are similar to other PCS patients undergoing surgery for other cardiac pathologies. Therefore, the concept whereby TAAD patients undergoing surgical repair and affected by PCS are at prohibitive risk for VA-ECMO should be challenged.

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Disclosures

The investigators have no conflicts of interest to disclose.

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Biancari and Mariscalco, had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Biancari, Mariscalco, Dalen, Fiore, Loforte, Spadaccio.
Acquisition of data: Alkhamees, Biancari, Bounaderm, Dalén, Dell'Aquila, El-Dean, Fiore, Gatti, Lichtenberg, Jónsson, Livi, Loforte, Mariscalco, Perrotti, Pettinari, Pol, Ragnarsson, Reichart, Ruggieri, Saeed, Settembre, Spadaccio, Welp.
Analysis and interpretation of data: Biancari, Mariscalco, Maselli.
Drafting of the manuscript: Biancari, Mariscalco, Maselli.
Critical revision of the manuscript for important intellectual content: Alkhamees, Biancari, Bounaderm Dalén, Dell'Aquila, Fiore, Gatti, Lichtenberg, Jónsson, Livi, Loforte, Mariscalco, Maselli, Perrotti, Pettinari, Pol, Ragnarsson, Reichart, Ruggieri, Saeed, Settembre, Spadaccio, Welp.
Paper supervision: Biancari, Mariscalco, Juvonen.
Statistical analysis: Biancari, Mariscalco.
Language revision: El-Dean.

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Table 1
Baseline characteristics

Variable†	TAAD (n=62)	No TAAD (n=719)	p value
Age (years)	62.9 ± 11.0	63.1 ± 13.1	0.58
Women	17 (27.4%)	232 (32.3%)	0.43
Body mass index (kg/m^2)	26.8 ± 5.0	27.2 ± 5.1	0.66
Presentation and cardiac status			
Urgent/emergent	55 (88.7%)	398 (55.4%)	<0.0001
Critical preoperative state	25 (40.3%)	251 (34.9%)	0.39
Preoperative stroke/unconsciousness	8 (12.9%)	19 (2.6%)	<0.0001
Prior cardiac surgery	14 (22.6%)	172 (23.9%)	0.81
Prior myocardial infarction	8 (12.9%)	191 (26.6%)	0.018
Comorbidities			
Diabetes mellitus	7 (11.3%)	193 (26.8%)	0.007
Haemoglobin (g/L)	123.1 ± 23.9	125.4 ± 21.8	0.89
Estimated glomerular filtration rate (mL/min/1.73 m^2)	66.3 ± 24.9	68.1 ± 30.7	0.79
Dialysis	3 (4.8%)	29 (4.0%)	0.74
Stroke	5 (8.1%)	55 (7.6%)	0. 91
Extracardiac arteriopathy	8 (12.9%)	110 (15.3%)	0.61
Pulmonary disease	10 (16.1%)	100 (13.1%)	0.63
Atrial fibrillation	13 (21.0%)	179 (24.9%)	0.49
PC-ECMO†, score	6.1 ± 3.2	3.7 ± 2.3	<0.0001
EuroSCORE 2, score (%)	15.3 ± 17.3	18.9 ± 15.6	0.003

TAAD, type A aortic dissection.

*Continuous data are presented as mean ± standard deviation; categorical variables as number (percent).

†PC-ECMO score is based on the following rik factors: age (60-69 tears, ≥70 years – points 2 or 4, respectively), female gender (points 1), prior cardiac surgery (points 1), arterial lactate ≥6 mmol/L (points 2), aortic arch surgery (points 4), and preoperative stroke/cuncounsciouness (points 5)[6].

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Table 2
Operative Data

Variable*	TAAD (n=62)	No TAAD (n=719)	p value
ACC time (minutes)	181± 238	122 ± 78	0.001
Median	139.5 (85)	106 (94)	
CPB time (minutes)	295 ± 117	218 ± 121	<0.0001
Median	218 (160)	277 (117)	
Surgical procedures			
Aortic procedures	62 (100%)	93 (12.9%)	<0.0001
Aortic root surgery	20 (32.3%)	67 (9.3%)	<0.0001
Isolated ascending aorta repair	33 (53.2%)	21 (2.9%)	<0.0001
Aortic arch repair	26 (41.9%)	13 (1.8%)	<0.0001
Aortic valve replacement/repair	9 (14.5%)	211 (29.3%)	0.008
Mitral valve surgery	2 (3.2%)	266 (37.0%)	<0.0001
Tricuspid valve surgery	-	100 (13.9%)	<0.0001
Coronary surgery	16 (25.8%)	374 (52.0%)	<0.0001
Other procedures	1 (1.6%)	74 (10.3%)	0.026
Timing of ECMO insertion			
VA-ECMO inserted immediately after surgery	46 (74.2%)	428 (59.5%)	0.023
Duration of ECMO support, days	5.1 ± 5.2	7.1 ± 6.3	0.003
Median	3.0 (7.0)	6.0 (7.0)	
Central arterial cannulation	19 (30.6%)	226 (31.4%)	0.99
Arterial lactate before VA-ECMO, mmol/L	6.8 ± 4.7	8.6 ± 4.8	0.002
Median	7.2 (4.8)	5.6 (6.3)	

ACC, aortic cross clamp; *CPB*, cardiopulmonary bypass; *VA-ECMO*, veno-arterial extracorporeal membrane oxygenation.

*Continuous data are presented as mean (standard deviation) and median (interquartile range); categorical variables as number (percent).

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Table 3 In-hospital Outcomes

Variable*	**TAAD** 62 pts	**No TAAD** 719 pts	**p value**
Primary end-point			
In-hospital mortality	46 (74.2%)	456 (63.4%)	0.089
Secondary end-points			
In-hospital mortality on VA-ECMO	41 (66.1%)	329 (45.8%)	0.002
Reoperation for bleeding/tamponade	30 (48.4%)	298 (41.5%)	0.29
Stroke/Global brain ischemia	21 (33.9%)	126 (17.6%)	0.002
Dialysis (new-onset)	34 (56.7%)	375 (53.1%)	0.59
Liver failure	19 (30.6%)	246 (34.3%)	0.56
Deep sternal wound infection	1 (1.6%)	28 (3.9%)	0.72
Blood stream infection	12 (19.4%)	167 (23.2%)	0.47
RBC > 9 units	48 (77.4%)	499 (69.5%)	0.19
RBC units transfused (units)	29.9 ± 21.0	23.1 ± 22.0	0.060
Median	20.0 (30)	15.0 (23)	
Pneumonia	17 (27.4%)	268 (37.3%)	0.12
Length of stay			
Intensive care unit stay (days)	11.9 ± 16.9	17.6 ± 18.3	<0.0001
Median	6.0 (14.0)	12 (19)	
Hospital stay (days)	16.6 ± 27.8	25.8 ± 31.7	<0.0001
Median	6.5 (15.0)	17.0 (27.0)	

VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

*Continuous data are presented as mean (standard deviation) or median [interquartile range]; categorical variables as number (percent)

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